

Appl. No. : 08/807,500
Filed : February 27, 1997

AMENDMENTS TO THE CLAIMS

1. **(Cancelled)**
2. **(Cancelled)**
3. **(Currently amended)** The first nucleotide sequence according to claim 10, wherein the virus second nucleotide sequence comprises the nucleotide sequence of a oncoselective autonomous parvovirus which is chosen from the group consisting of parvovirus H1, fibrotropic parvovirus variant of Minute virus of Mice (MVMp) and parvovirus LuIII.
4. **(Currently amended)** The first nucleotide sequences sequence according to claim 10, wherein the virus second nucleotide sequence comprises a nucleotide sequence of an oncoselective autonomous parvovirus which lacks nucleotide sequences encoding the parvovirus capsid proteins VP1 and VP2.
5. **(Currently amended)** The nucleotide sequence according to claim 4, further comprising inserted between the a promoter P4 and a non-structural protein NSI, a promoter which is activated in target cells.
6. **(Currently amended)** The nucleotide sequence according to claim 4, wherein the virus nucleotide sequence of the oncoselective autonomous parvovirus further lacks the a nucleotide sequence of the a promoter P38 and the nucleotide sequences encoding the parvovirus nonstructural proteins NSI and NSII.
7. **(Currently amended)** The first nucleotide sequence according to claim 4 or 10, wherein said third nucleotide sequence comprises an the effector nucleotide sequence which comprises at least two coding nucleotide sequences, at least two non-coding nucleotide sequences, or combinations thereof, operably linked in polycistronic subunits under the control of a single promoter unit.
8. **(Original)** The nucleotide sequence according to claim 7, wherein the effector nucleotide sequence is between two coding nucleotide sequences and the effector nucleotide sequence comprises one IRES nucleotide sequence.
9. **(Currently amended)** The first nucleotide sequence according to claim 10, wherein the third nucleotide sequence comprises an effector nucleotide sequence which encodes at least one fusion polypeptide containing at least one ligand selected from the group consisting of the a hypervariable end specific of an antibody, a cytokine and a growth factor, wherein the

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ligand binds specifically to at least one molecule expressed at the surface of cancerous or infected cells.

10. (Currently amended) A first nucleotide sequence comprising the a second nucleotide sequence and a third nucleotide sequence, said second nucleotide sequence comprising the nucleotide sequence of an oncoselective autonomous parvovirus, and said third nucleotide sequence comprising at least one effector nucleotide sequence encoding an effector polypeptide which, wherein said effector polypeptide effects the destruction or the normalization of cancer cells,

wherein the effector nucleotide sequence comprises at least one sequence chosen from the group consisting of ~~the nucleotide sequences that encode~~:

- a nucleotide sequence that encodes a cytotoxic polypeptide or at least one fragment of this polypeptide,
- a nucleotide sequence that encodes a molecule which confers on the a transfected cell sensitivity to a radioactive toxic agent,
- a nucleotide sequence that encodes at least one polypeptide which increases an immune response, and
- a nucleotide sequence that encodes at least one polypeptide or a fragment of this polypeptide which inhibits tumor neoangiogenesis.

11. (Currently amended) The first nucleotide sequence according to claim 10, wherein the fragment of the cytotoxic polypeptide encoded by said effector nucleotide sequence is fragment A of diphtheria toxin.

12. (Currently amended) The first nucleotide sequence according to claim 10, wherein the molecule encoded by the effector nucleotide sequence is Herpes simplex virus type 1 thymidine kinase (HSV-TK), and the radioactive toxic agent is a guanosine analog labeled with the aid of a radioisotope which emit emits Auger electrons such as 123 Iodine.

13. (Currently amended) The first nucleotide sequence according to claim 10, wherein the polypeptide capable of inhibiting which inhibits tumor neoangiogenesis is selected from the group consisting of interferon- α , interferon- β and platelet factor 4.

14. (Currently amended) The first nucleotide sequence according to claim + 10, wherein the effector nucleotide sequence comprises at least one nucleotide sequence which can be transcribed into an RNA, which destroys or normalizes cancer cells or infected cells.

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15. **(Currently amended)** The nucleotide sequence according to claim 14, wherein the nucleotide sequence ~~that which~~ can be transcribed into an RNA which destroys or normalizes cancer cells or infected cells is an antisense RNA or a ribozyme.

16. **(Currently amended)** The first nucleotide sequence according to claim + 10 which further comprises at least one regulatory nucleotide sequence activated by transactivation factors specific for a medical condition and/or for the affected cellular tissue and which cisactivates the effector nucleotide sequence.

17.-20 **(Cancelled)**

21. **(Currently amended)** The nucleotide sequence according to claim 16, wherein the regulatory nucleotide sequence contains at least one promoter and/or at least one enhancer ~~transactivatable~~ transactivatable in certain specific tissues and chosen from the group consisting of:

- the nucleotide sequence controlling the expression of the gene encoding α-fetoprotein (AFP),
- the nucleotide sequence controlling the expression of human placental protein 11 (PP11),
- the nucleotide sequence controlling the expression of antigen CO-029,
- the nucleotide sequence controlling the expression of antigen H23,
- the nucleotide sequence controlling the prostatic expression of prostatic secretory protein PSP94,
- the nucleotide sequence controlling the expression of the protein pHGR11 associated with melanoma, ovarian cancer, adenocarcinoma of the colon and of the prostate,
- the nucleotide sequence controlling the expression of protein pHGR74, expressed in the testicles, the prostate, the seminal vesicle and the granulosa of the ovary,
- the sequences controlling the expression of proteins specific for the mammalian epithelium, ~~for the uterine epithelium~~,
- the nucleotide sequence controlling the expression of tyrosinase, expressed in the melanocytes and malignant melanoma,
- the nucleotide sequences controlling the expression of elastase, expressed only in the exocrine pancreas,

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-the nucleotide sequence controlling the hypophysial expression of prolactin,
and/or

-a mixture thereof.

22. (Currently amended) The A recombinant vector comprising the sequence or a portion of the first nucleotide sequence according to claim 10.

23.-27 (Cancelled)

28. (Currently amended) A nucleotide sequence comprising the nucleotide sequence of an autonomous parvovirus, and at least one effector nucleotide sequence encoding a polypeptide which effects the destruction or normalization of cells infected by intracellular infectious parasites,

wherein the effector nucleotide sequence comprises at least one sequence selected from the group consisting of ~~nucleotide sequences that encode~~:

-a nucleotide sequence that encodes a cytotoxic polypeptide or at least one fragment of this polypeptide,

-a nucleotide sequence that encodes a molecule which confers on ~~the a~~ transfected cell sensitivity to a radioactive toxic agent, and

-a nucleotide sequence that encodes at least one polypeptide which increases an immune response.

29. (New) The nucleotide sequence of Claim 21, wherein said mammalian epithelium is uterine epithelium.

30. (New) The nucleotide sequence of Claim 12, wherein said radioisotope is ¹²³Iodine.